

Title (en)
COMPOSITIONS AND METHODS FOR IMPROVING BASE EDITING

Title (de)
ZUSAMMENSETZUNGEN UND VERFAHREN ZUR VERBESSERTEN BASISBEARBEITUNG

Title (fr)
COMPOSITIONS ET PROCÉDÉS D'AMÉLIORATION DE L'ÉDITION DE BASE

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Application
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Abstract (en)
[origin: WO2020051562A2] The invention features compositions and methods for modifying a polynucleotide (e.g., DNA) using a nucleobase editor comprising a first DNA binding protein domain that is catalytically inactive, a domain having base editing activity, and a second DNA binding protein domain having nickase activity, where the DNA binding protein domains are expressed as a single fusion protein or are expressed separately (e.g., on separate expression vectors). The invention also features a fusion protein comprising a domain having base editing activity (e.g., cytidine deaminase or adenosine deaminase), and two nucleic acid programmable DNA binding protein domains (napDNAbp), a first napDNAbp comprising nickase activity and a second napDNAbp that is catalytically inactive, where at least the two napDNAbps are joined by a linker. In one embodiment, the fusion protein comprises a DNA binding domain of a CRISPR-Cas having nickase activity (nCas; e.g., nCas9), a catalytically inactive DNA binding domain of CRISPR-Cas (dCas; e.g., dCas9), and a deaminase domain, where the dCas is joined to the nCas by a linker, and the dCas is immediately adjacent to the deaminase domain, as well as related methods for using such base editors, and kits comprising the base editors.

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